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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,935	04/25/2005	Randy S. Seeley	10738-37	6972

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/506,935	SEELEY, RANDY S.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendment of 8/31/06 is entered.

Claims 1-13 are presently pending.

Note: Claim Amendments

Applicant's claims fail to comply with 37 CFR 121(c), which requires that all claims be properly identified with claim identifiers, and marked properly to demonstrate any amendments. However, in the interest of compact prosecution, the Examiner has entered the claims as presented. The Examiner understands there exists no amendments to the claims, and if such is incorrect, the Examiner further requests clarification.

However, Applicant is further notified that future claim amendments that are improperly marked will be responded to with a notice of non-compliance.

Election/Restrictions

Applicant's election with traverse of the species of hypothalamus, isolation of RNA, and statistical analysis in the reply filed on 8/31/06 is acknowledged. The traversal is on the ground(s) that (i) RNA, DNA and protein expression are interrelated, and (ii) a search of all bioinformatics methods would not be unduely burdensome, considering that researchers use a number of methods in any particular analysis.

With regard to (i), such is not persuasive, because they require distinct materials and method steps which are non-coextensive, and while the various levels of expression are interrelated, they do not predict each other in any specific case.

With regard to (ii) the requirement is withdrawn because all bioinformatics analyses are statistical methods.

It is noted that Applicant has not traversed the requirement for a specific tissue, and hence, the hypothalamus is treated as not traversed as no argument has been supplied.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-13 are considered with respect to the elected species.

Claim Rejections - 35 USC § 112 - clarity

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: those steps required to obtain from the expression of a gene or a protein expression identified to determine a therapeutic strategy. Such missing step(s) make the claim unclear.

Claims 1 and 13 each recite "therapeutic strategies". The metes and bounds of such are unclear, as the strategy does not identify what the strategy is therapeutic for.

Claims 1 and 13 each recite "a prolonged overfeeding regimen". The metes and bounds of such limitation are unclear. While the specification discloses specific embodiments, no specific definition is provided as to the minimal requirement of such overfeeding regimen encompasses. Hence, while the specification defines at least 3 days as being the minimal period,

in one specific embodiment, it is still unclear if the prolonged feeding regimen may encompass 1 day, 1 hour, or less.

Claims 1 and 13 each recite "identifying gene and/or protein expression that occur ... with the prolonged feeding regimen". However, Claim 4 limits the limits the identification to occurring during and/or after the prolonged overfeeding regimen. Such limitation makes it clear that the term "with" is meant to encompass more than during or after the overfeeding regimen, which is inconsonant with that of the normally accepted meaning of the term "with".

Claims 2-12 are rejected as being dependent on a rejected base claim, and not overcoming the lack of clarity in such base claim.

Claim Rejections - 35 USC § 112 – written description

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-13 encompass the generic determination of a generic therapeutic strategy.

The specification discusses overfeeding of animals and determining levels of gene or protein expression. Further, the therapeutic strategy, at best, is only referred to as using the methods (e.g., p. 5, paragraph 2).

The art, while teaching many specific protocols for particular disorders, which may require various drugs and/or other nutrients and excercises, similarly does not teach a generic therapeutic strategy and how to obtain one from the identification of a gene expression.

Hence, the Artisan would not have understood Applicant to have been in possession of a generic method for determining a therapeutic strategy at the time of filing.

Therefore, these claims are rejected for lacking written description.

It is noted that the following art rejections even in light of the lack of enablement, and they are applied because of the breadth of Applicant's claims as well as the fact that the Art does not require the claimed invention to be enabled or patentable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 6-8, and 9-13 rejected under 35 U.S.C. 102(a), and under 35 U.S.C. 102(e), as being anticipated by US Patent Publication No. 2002/0041870 to Wu, published 4/11/02, claiming priority to 7/26/00.

With regard to Claim 1, 4, and 13, Wu teaches identification of differentially expressed genes in the hypothalamus due to overfeeding regimens (EXAMPLE 1). Further, the various methods for producing overfed animals describe providing diets over 100% of normal diet (paragraph 0151).

With regard to Claim 6-8, Wu describes identifying the gene expression in the hypothalamus (EXAMPLE 1; paragraph 00293).

With regard to Claim 9, Wu describes isolating RNA and analyzing the levels of expression of such RNA (paragraphs 0154-0155), and further, that the RNAs expressed are selected based on the level of expression (e.g., paragraph 0293), which necessarily defines the target.

With regard to Claims 11-12, Wu's specific example is inherently a statistical analysis of the expression differences of RNAs in the hypothalamus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Publication No. 2002/0041870 to Wu, published 4/11/02, claiming priority to 7/26/00, and Hagan, et al. (1999) J. Neuroscience, 19(6): 2362-67.

With regard to Claim 1, as noted above, Wu teaches the various aspects. However, Wu does not teach the method of overfeeding using a gastric catheter or the measurement of levels of gene expression prior to the overfeeding.

However, Hagan teaches the use of a gastric catheter in overfeeding regimens in analyzing CNS RNA levels, which includes the hypothalamus (e.g., ABSTRACT; p. 2363, col. 1, paragraph 1). Moreover, Hagan teaches that expression levels obtained prior to the overfeeding regimen may be used.

At the time of the invention, it would have been obvious to modify the methods of Wu to use the gastric catheter and obtain measurements of expression prior to overfeeding, as taught by Hagan, in overfeeding an animal. The Artisan would have been motivated to do so because the catheter would provide specific control of caloric intake, and Hagan had demonstrated that obtaining such parameters prior to overfeeding would provide an adequate control. Moreover, the Artisan would have had a reasonable expectation of success, as Hagan had demonstrated the catheter feeding useful for controlling caloric intake, and the prior obtained gene expression to be a useful control.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Publication No. 2002/0041870 to Wu, published 4/11/02, claiming priority to 7/26/00, and Rast, et al. (2000) Dev. Biol., 228: 270-86.

As noted above, Wu anticipates, and therefore also obviates Claims 1 and 9, however, Rast does not teach the making of a probe array prepared from the RNAs, and using such to analyze RNA expression. On the other hand, Wu recognizes that any method of high-throughput analysis may be used (e.g., paragraphs 0195-0199).

Further, Rast demonstrates the manufacture of arrays from RNAs, to analyze gene expression (e.g., ABSTRACT).

Hence, it would have been obvious to modify the methods of Wu with the arrays as taught by Rast, at the time of invention. The Artisan would have been motivated to do so in order to test many discreet RNAs at once, quickly, as outlined by Wu (paragraph 0195). Moreover, the Artisan would have had a reasonable expectation of success, as Wu had taught that these high-throughput methods could be used, and Rast had demonstrated that the arrays were known to be useful in the Art.

Claim Rejections - 35 USC § 112 – enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-12 encompass a method of determining any therapeutic strategy and/or any target for examining any weight loss in any animal, comprising administering any prolonged overfeeding regimen and any identification and/or protein expression that occur in the individual with the overfeeding regimen. Claims 2-3 require the individual be fed by direct administration of calories to the stomach, which may be through a gastric catheter. Claims 4-5 require gene expression to be identified during or after the prolonged overfeeding regimen. Claims 6-8 require that the gene expression be identified through a tissue sample, which includes the use of hypothalamus, as the elected species. Claims 9-12 require, with respect to the elected invention,

that identification of gene/protein expression be identified through collecting a tissue sample, isolating RNA, determining a level of expression of the RNA, analyzing the expression, and defining a target based on the analysis. Claims 10 limits the step of determining the level of expression to preparing any probe using the RNA, applying the probe to an array, and measuring the level of the RNA. Claims 11-12 limit the analyzing of the level of expression to several methods under the broad class of bioinformatics analysis or combinations thereof.

Claim 13 parallels that of Claim 1, but requires the targets to be for wasting disorders, rather than weight loss.

These claims are broad for determining any therapeutic strategy, determining any target for any examining of any weight loss, determining any target for any wasting disorder, any prolonged overfeeding regimen, any identification at any time before/during/after the overfeeding regimen, determining gene expression, and any animal.

The Nature of the Invention

The nature of the invention is identifying a therapeutic strategy and/or targets for examining weight loss and/or targets for wasting disorders, through providing an overfeeding regimen and identifying gene expression in an individual.

The nature of such identification of therapeutic strategy is necessarily not reasonably predictable. To wit, the result is identification of the expression of a gene in an individual, however, such does not equate to weight as simply finding a gene would require further experimentation to determine how to use such gene in any particular therapeutic strategy to effect any particular therapeutic strategy, examination of weight loss, or to effect or counteract any particular wasting disorder in any particular animal.

Further, the nature of science demonstrates that various aspects of the invention as claimed are not reasonably predictable. To wit, the mere identification of gene expression, rather than a controlled determination of changes in gene expression due to overfeeding, would only identify genes, rather than genes correlating with overfeeding, as many genes are necessarily unaffected, and do not effect any responses to overfeeding. Hence, because Applicant's claims do not require a controlled comparison of gene expression levels to unaffected individuals, it is not reasonably predictable that any particular gene obtained would be correlated to overfeeding, much less any therapeutic strategy, examining weight loss, or wasting disorder, in any particular animal.

The State of the Prior Art

The prior art has consistently demonstrated that it is not reasonably predictable that any particular gene, once identified, would be predictive for any particular therapeutic strategy, or examining any particular disorder, once identified.

To wit, similar gene discovery methods have been well-known to not produce reasonably predictable markers for their particular disorders or therapy. The Artisan is painfully aware that gene association studies are typically wrong, as reviewed by Lucentini (2004) "Gene Association Studies are Typically Wrong", The Scientist, 18(24): 20. Lucentini discusses that in a particular study by Crocq's, where genes were located that appeared to be quite clearly associated with a disease, were subsequently found to be completely wrong, and even today, Lucentini does not understand what is going on, after much research (Article in general). Moreover, "Experiences like Crocq's, in which follow-up studies overturn an initial finding of a gene-disease association, are strikingly common, researchers say. Two recent studies found that typically, when a finding

is first published linking a given gene with a complex disease, there is only a roughly a one-third chance that studies will reliably confirm the finding. When they do, they usually find the link is weaker than initially estimated" (p. 20, col. 1, paragraph 3). Hence, even if the results obtained were as well determined as Crocq's, only a 30% chance exists that the gene would be differentially-expressed in any particular disorder.

Hence, because it is well known that gene association studies are not reasonably predictable of any particular marker of any particular disease, the Artisan would have to experiment further upon obtaining such a marker to reasonably confirm the association of any particular marker with any particular weight loss, wasting disorder, or therapeutic strategy.

Further, even once a marker has been completely associated with any particular weight loss or wasting disorder, the Artisan would have to experiment to determine whether such gene could be targeted in any particular therapeutic strategy to obtain any particular therapy. To wit, with regard to a well-recognized marker of obesity, leptin, the art generally recognizes that the results with treatment with leptin are specious at best, and was not reasonably predicted by the Artisan to be efficacious for any particular obesity/unwanted body mass at the time of filing. To wit, Buettner, et al. (2000) Am. J. Physiol. Endocrinol. Metab., 278: E563-69 report "the ability of leptin administration to reverse metabolic abnormalities in the ob/ob mouse and improve insulin action in normal animals has lead to the proposal that leptin may serve as an effective therapy for human obesity." Buettner goes on to caution that before leptin can effectively be used to treat obesity a number of questions remain to be answered. "First, it is not clear that increasing plasma leptin levels will be sufficient to correct the metabolic abnormalities associated with obesity, principally insulin resistance and perturbed lipid and carbohydrate

metabolism. Second leptin therapy involving multiple injections has had mixed results both in animal models of obesity and in human trials, and this suggests that alternative strategies such as sustained increases in plasma leptid should be considered." (p. E556). Moreover, Chiesi, et al. (2005) Trends in Pharmacol. Sci., 22(5): 247-54 provides a recent review of the field, demonstrating that such therapies with leptin are similarly not even now considered to be reasonably predictable. To wit, Chiesi discusses the discovery of leptin, its nature as a feedback regulator, and mouse models which seemed to indicate that it would treat obesity, followed by a small trial where a patient was treated (p. 247, paragraph bridging columns). However, subsequent clinical trial indicated leptin was much less promising than expected (Id., col. 2, paragraph 2), where, even after extremely high doses, weight loss was variable, and average reductions in weight were small (Id.). The author explains many reasons why such results may be found, including, for example, leptin's activity may be at very low concentrations, and increases have no effect, therapeutic efficacy may have been overestimated, human responses are not the same as the mouse, some humans may be resistant to leptin, either due to leptin receptor signaling or transportation of leptin in the body (p. 247, col. 2, paragraph 3). Moreover, Liu, et al. (2005) Drugs of Today, 41(5) : 345-62 adds another complication: obesity and unwanted body mass are actually unlike other genetic diseases, being under the control of many genetic factors (p. 351, col. 2, paragraph 2). Hence, from this, the Artisan could not reasonably predict that any particular obesity or wasting disorder could be examined or treated, much less detected before obesity occurs such that treatment could be effected, because the mechanisms involved are simply not understood well enough.

Hence, the Artisan generally recognizes that any particular gene, once identified as associated with any particular weight disorder, would have to perform more research to reasonably confirm that such gene is linked to the weight disorder, much less to any other weight disorder. Further, the Artisan in weight disorder research generally recognizes that even if a gene is specifically linked to any weight disorder, it is not reasonably predictable that it is linked to all weight disorders, or that any particular therapeutic strategy would be efficacious when using such gene as a target for such therapy. Hence, such would require further research.

The Direction and Guidance Provided by Applicant

Applicant's specification broadly discusses a gene discovery method, overfeeding, and weight disorders.

However, such broad description does not provide the specific direction and guidance the Artisan would require to reasonably determine that these obtained genes would be marker for examining weight loss, for weight disorders, or in any therapeutic strategy. To wit, Applicant has not identified why Applicant's methods are applicable to the broad classes provided, and the Art, as shown above, has demonstrated that the mechanisms involved are generally not known. Moreover, the Art has demonstrated that any particular identification, once made, may not actually be linked to the disorders, much less the therapies.

The Existence of Working Examples

Applicant's example demonstrates a single experiment where various rats are given controlled diets, and fed by gastric catheter, and gene expression differences are analyzed.

However, in addition to not providing any more reasonable predictability than the art, also is not commensurate with that of the claims in that the expressed genes are taken in a

comparison with that control fed animals. Hence, even Applicant provides the controls required to reasonably determine a change in gene expression rather than simply identifying any and all gene expression.

The Level of Skill in the Art

The level of skill in the Art is high, however, even the Artisan does not know the mechanisms involved in any particular weight disorder, as evidenced by the Art, and therefore even the Artisan would not find Applicant's claims enabled.

The Level of Predictability in the Art

It is noted that the Artisan does not find this art predictable, as demonstrated by the Art cited.

Undue Experimentation

The Artisan would have to experiment to find the proper controls for the experiments, to determine if any gene found is linked to any particular disorder, and to determine a therapeutic strategy using such gene found. Such experimentation is undue because it amounts to inventing Applicant's invention for Applicant.

Conclusion

Because of the finding of undue experimentation, the invention is not enabled.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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